

**PATENT COOPERATION TREATY**

BLAKE DAWSON WALDRON  
PATENT SERVICES

**COPY**

RECEIVED: 31 MAR 2005  
**DATA ENTERED**

**PCT**

From the:  
INTERNATIONAL SEARCHING AUTHORITY

To:

Blake Dawson Waldron  
Level 39  
101 Collins Street  
MELBOURNE VIC 3000

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing  
(day/month/year)

17 MAR 2005

**FOR FURTHER ACTION**

See paragraph 2 below

Applicant's or agent's file reference

WJP DAAS 03 1378 8838

International application No.

**PCT/AU2005/000022**

International filing date (day/month/year)

12 January 2005

Priority date (day/month/year)

12 January 2004

International Patent Classification (IPC) or both national classification and IPC

Int. Cl. <sup>7</sup> C07D 403/04, 403/14, 401/04, 407/14, 409/14, 413/14; A61K 31/497, 31/4439, 31/506; A61P 37/06

Applicant

**CYTOPIA RESEARCH PTY LTD et al**

1. This opinion contains indications relating to the following items:

- |                                     |              |  |
|-------------------------------------|--------------|--|
| <input checked="" type="checkbox"/> | Box No. I    | Basis of the opinion   |
| <input type="checkbox"/>            | Box No. II   | Priority   |
| <input checked="" type="checkbox"/> | Box No. III  | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability   |
| <input type="checkbox"/>            | Box No. IV   | Lack of unity of invention   |
| <input checked="" type="checkbox"/> | Box No. V    | Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/>            | Box No. VI   | Certain documents cited  |
| <input type="checkbox"/>            | Box No. VII  | Certain defects in the international application   |
| <input checked="" type="checkbox"/> | Box No. VIII | Certain observations on the international application  |

**2. FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the IPEA/AU

AUSTRALIAN PATENT OFFICE  
PO BOX 200, WODEN ACT 2606, AUSTRALIA  
E-mail address: pct@ipaaustralia.gov.au  
Facsimile No. (02) 6285 3929

Authorized Officer

**R.L. POOLEY**

Telephone No. (02) 6283 2242

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

**PCT/AU2005/000022**

**Box No. I**

**Basis of the opinion**

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.  
☐ This opinion has been established on the basis of a translation from the original language into the following language \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material  
☐ a sequence listing  
☐ table(s) related to the sequence listing
  - b. format of material  
☐ in written format  
☐ in computer readable form
  - c. time of filing/furnishing  
☐ contained in the international application as filed.  
☐ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/AU2005/000022

**Box No. III**      **Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos: 1-9 (in part)

because:

☐ the said international application, or the said claim Nos.

relate to the following subject matter which does not require an international preliminary examination (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos.  
are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos.  
are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 1-9 (in part)

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form ☐ has not been furnished

☐ does not comply with the standard

the computer readable form ☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See Supplemental Box for further details.

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

**PCT/AU2005/000022**

**Box No. V**

**Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Claims	YES
	Claims 1-9	NO
Inventive step (IS)	Claims	YES
	Claims 1-9	NO
Industrial applicability (IA)	Claims 1-9	YES
	Claims	NO

**2. Citations and explanations:**

The following documents were cited in the International Search Report:

D1 – WO 2003/099811

D2 – WO 2001/000213

**NOVELTY (N) and INVENTIVE STEP (IS)**

Both of the above documents D1 and D2 disclose compounds that overlap with the compounds defined in the present claims. They also disclose pharmaceutical compositions containing these compounds and their use in the treatment of immunosuppressive diseases.

Document D1 discloses a range of compounds wherein substituent group A of the present formula I is pyrazine. There is significant overlap between the compounds disclosed in document D1 when substituent D of document D1 is the first mentioned option and R2 is NR<sub>3</sub>COR<sub>4</sub>, C<sub>1-4</sub>alkylNR<sub>3</sub>COR<sub>4</sub>, NR<sub>3</sub>SO<sub>2</sub>R<sub>4</sub> and C<sub>1-4</sub>alkylNR<sub>3</sub>SO<sub>2</sub>R<sub>4</sub>. For example, the compounds of examples 107, 108 and 193 fall within the scope of the present claims. Accordingly claims 1-9 are considered to lack novelty and inventive step in light of document D1.

Document D2 discloses a range of compounds wherein substituent group A of the present formula I is pyrimidine. There is significant overlap between the compounds disclosed in this document and those of the present claims, particularly when the R<sup>6</sup> and R<sup>6a</sup> substituents of document D2 are groups (i), (k), (p), (s), (ab) and (aj) (see pages 7-8). For example, the compounds of examples 82, 83, 85-92, 111, 112, 130-135, 138, 139, 143-151, 167-170 and 175-181 fall within the scope of the present claims. Thus claims 1-9 are also considered to lack novelty and inventive step in light of document D2.

**INDUSTRIAL APPLICABILITY (IA)**

Claims 1-9 are considered to possess industrial applicability.

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

**PCT/AU2005/000022**

**Box No. VIII      Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

- (i) Claims 1 and 2 are not fully supported by the description because they include compounds which have not been exemplified and which could differ significantly in structure from the compounds that have been made. As a consequence of these significant structural differences, it is considered that some of the compounds falling within the scope of the above claims represent an unreasonable extrapolation from what has been exemplified in the description. In particular, the examples do not contain any instances wherein substituent A is the last 3 heterocyclic moieties of claims 1 and 2. In addition, many of the substituents defined for the variable Z have also not been exemplified – the examples appear to only exemplify compounds wherein a nitrogen atom is the first atom in substituent Z. Thus it is considered that a significant proportion of the claimed compounds are not represented in the examples and that the compounds of claims 1 and 2 constitute an unreasonable extrapolation from what has been done.
- (ii) Claim 3 is not fully supported by the description because it includes compounds that do not fall within the scope of claims 1 and 2 and because it also includes several compounds that have not been described in the description. For example, the 3<sup>rd</sup> compound at page 75, last line, the 3<sup>rd</sup> compound at page 76, 4<sup>th</sup> line, the 4<sup>th</sup> compound at page 76 6<sup>th</sup> line, the 2<sup>nd</sup> compound at page 77, 2<sup>nd</sup> line and the 4<sup>th</sup> compound at page 77 6<sup>th</sup> line would all seem to be outside the scope of claim 1. Furthermore, claim 3 also includes compounds wherein R9 is outside the scope of compounds defined in claim 1. For example, the compounds at page 75, last line, 3<sup>rd</sup> compound and page 76, 1<sup>st</sup> line, last compound appear to have a pyridine ring directly attached as substituent R9, but R9 and R10 can only be C<sub>1-4</sub>alkylhetaryl as defined in claim 1.

In addition, claim 3 includes several compounds that have not been specifically described or exemplified in the description – the 1<sup>st</sup> and 4<sup>th</sup> compounds at page 75 line 3 are examples of such compounds.

- (iii) Claim 1 is unclear because it contains two options numbered (ii) in the definition of substituent W.